ARS Partners With Defense Department To Protect Troops From Insect Vectors

One chapter in the history of American warfare that should not be overlooked is the epic battles with insect pests and the deadly diseases that some are capable of transmitting to U.S. combat forces.

Known as "vectors," mosquitoes, fleas, mites, lice, and flies pose a threat of disease that can seriously hamper military operations.

It's little wonder, then, that the U.S. military has been a leader in research on preventing these diseases. What is not widely known is the role USDA scientists have played to support their work. From the discovery that DDT could prevent louse-borne typhus to the recent invention of a new class of mosquito repellent, USDA's Agricultural Research Service has helped prevent insect-borne diseases in both our military and civilians.

"Many of the most important products in use today to control disease-carrying insects were developed as a result of the relationship between USDA and the U.S. military," says Navy Captain Gary Breeden, research liaison officer of the Armed Forces Pest Management Board, located in Silver Spring, Maryland.

Breeden points out that the threat to the U.S. military exists not only during combat but also during peacekeeping and training missions. Indeed, it is as real today as it was 50 years ago, and in some ways worse. For instance, malaria is the single most important parasitic infectious disease in the world, killing more than one million children in Africa each year. Although researchers have learned many ways to control the spread of malaria during military operations, it remains a threat because the *Anopheles* mosquito is becoming increasingly resistant to available insecticides. In 2003, about 80 Marines and Navy corpsmen from Joint Task Force-Liberia contracted malaria during the few days they were ashore evacuating Americans. And service members deploying for Iraq and Afghanistan today learn a new word for an unusual danger: Leishmaniasis. This blood parasite kills more than 200,000 people per year and infects more than 10 million, mainly in Asia, Africa, and Latin America. The only way to contract leishmania parasites is through the bite of the tiny sand fly. The disease can occur as a skin, or cutaneous, form, known as "Baghdad boil" to troops in Iraq, and a more deadly internal, or visceral, form. The disease can be treated, but only by prolonged and uncomfortable therapy.

The partnership between USDA and the Department of Defense

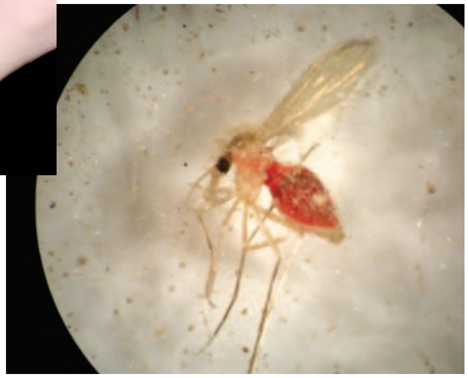
CENTERS FOR DISEASE CONTROL (D205-1)

***Anopheles freeborni* mosquito.**

WALTER REED ARMY INSTITUTE OF RESEARCH (WRAIR) (D202-1)

Cutaneous leishmaniasis, a skin form of the disease transmitted by sand flies.

WRAIR (D201-1)



Engorged sand fly (about 2 cm long).

TIMELINE: Past breakthrough scientific achievements from USDA/DOD partnership

• From 1942 to 1944, USDA was involved in creating delousing preparations that led to saving thousands of U.S. troops from deadly typhus—and ultimately about 25 million people worldwide.

JACK ROSEBUSH (D204-1)

Delousing operation—World War II, Italy 1944.

• USDA scientists in Orlando, Florida, demonstrated that DDT killed lice that transmit typhus and fleas that transmit plague. The scientists discovered it had "residual qualities" that kept it effective for weeks or months after being applied to fabric. The World Health Organization estimated that widespread use of DDT prevented more than 25 million deaths from malaria following World War II.

• USDA researchers Lyle Goodhue and William Sullivan invented the aerosol spray canister, dubbed the "bug bomb," to dispense insecticides. The design, patented in 1943, is the ancestor of many popular commercial spray products. Pressurized by liquefied gas, which gave it propellant qualities, the small, portable can enabled soldiers to defend against malaria-carrying bugs by spraying inside tents during World War II. Propellents used in these older aerosol cans have since been replaced with environmentally friendly ones.

• USDA scientists at the Bureau of Entomology and Plant Quarantine lab in Orlando (precursor to CMAVE at Gainesville)

(D200-2)

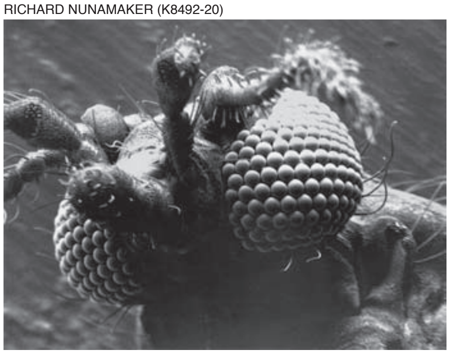
Aerosol spray canister invented by USDA researchers.

(DOD) is well established and time honored. In 1944, General George C. Marshall, then Army Chief of Staff, instituted the first formal collaboration, which has been continually renewed to this day. Most recently, USDA has begun a new DOD-funded program to develop a new generation of tools to protect our military from disease-transmitting insects. This initiative, “Deployed War-Fighter Protection Against Disease-Carrying Insects,” began with projects at five ARS research units. The emphasis is on identifying and testing new classes of pesticides aimed at disease vectors, new tools for pesticide application suited to the military environment, and new methods for personal protection.

The Search for New Chemical Tools

A medical entomology unit was created by USDA during World War II in Orlando, Florida, to develop methods for stopping transmission of insect-borne diseases. It was there that DDT—which had been discovered in Switzerland years before but never used—was demonstrated to kill lice that transmit epidemic typhus and fleas that transmit plague. Using this knowledge, ARS and military entomologists came up with a system for mass delousing of civilian populations. This plan was first put into action in Sicily, where it has been credited with preventing an epidemic of typhus that would have sickened and killed thousands.

RICHARD NUNAMAKER (K8492-20)



Blood-feeding midge, *Culicoides sonorensis,* the vector of Oropouche and other viruses. Magnified about 46x.

With repeated exposure to an insecticide, insect pests can develop resistant populations. That fact, as well as environmental concerns, has pushed American agriculture toward integrated pest management (IPM) programs, which minimize use of chemical pesticides. But IPM requires time and planning not available to military preventive-medicine officers, who must work not only fast but also in the most hazardous and limiting of conditions. For them, chemical pesticides are usually the most effective weapons.

(K1654-18)

In 1984, ARS technicians Kenneth Posey (left) and Dick Godwin conduct a field test in a Florida woodland of mosquito repellents on skin and in military uniforms.

ARS scientists at the Mosquito and Fly Research Unit, of the Center for Medical, Agricultural, and Veterinary Entomology (CMAVE) in Gainesville, Florida, are literally laying the foundation for a long-term program to identify and test potential successors to DDT for military use: They’re overseeing construction of a

SCOTT BAUER (K7243-7)

Insect repellents made from DEET, an ARS-developed compound.

tested and reported the repellent properties of DEET. Beltsville scientists published additional findings in 1954 and registered DEET for public use. Today, billions of doses of DEET are being used worldwide in varying concentrations and forms, including gels, aerosol and pump sprays, sticks, and lotions.

• Military adapts ultra-low-volume (ULV) equipment in 1960 as part of efforts to improve flying-insect control. ULV foggers use a high volume of air at low pressure to generate fog droplets containing pesticide. It’s considered the most efficient way of killing adult mosquitoes. Developed by CMAVE scientists, the method greatly reduces the amount of pesticide dispersed in outdoor applications.

• From the 1960s to the 1980s, Carl Schreck of CMAVE was a pioneer in development of permethrin-treated military uniforms and bed nets that repel ticks and kill disease-carrying mosquitoes, saving millions of people from malaria.

CMAVE (D206-1)

ARS researcher Gary Mount operates experimental truck-mounted ultra-low-volume equipment during a 1967 trial.

state-of-the-art insectary for production of the thousands of mosquitoes of several species that will be needed each week. When completed, this facility will be the finest of its kind in North America.

Meanwhile, both at CMAVE and at the Chemicals Affecting Insect Behavior Laboratory (CAIBL) in Beltsville, Maryland, ARS scientists are forming partnerships with universities, industry, and the World Health Organization to develop sophisticated procedures for selecting promising insecticide candidates from thousands of compounds already in company inventories. The ideal insecticide for military use will be fast acting against adult mosquitoes and flies, moderately persistent, easy to store and apply, not toxic to vertebrates, and slow to cause resistance—characteristics that would also be valuable in preventing epidemics among civilian populations.

Controlling house flies and other filth-breeding flies that carry intestinal bacteria onto food and skin, however, requires a different approach. Ronald J. Nachman, a chemist at the Southern Plains Agricultural Research Center in College Station, Texas, is developing ways to transport molecules that mimic hormones across the water-impermeable membrane of maggots; the goal will be agents that remain active for long periods in breeding places.

To be useful, pesticides and repellents must work against not only mosquitoes but also other disease-transmitting arthropods. Edward T. Schmidtman, an entomologist at the Arthropod-Borne Animal Diseases Research Laboratory in Laramie, Wyoming, will conduct testing against the tiny blood-feeding midge, *Culicoides,* the vector of Oropouche and other viruses. Jerry Hogsette, an entomologist at CMAVE, will do the same for house flies, which spread a variety of diarrheal agents. Sand flies—the vectors of leishmaniasis—will be supplied from colonies at the Walter Reed Army Institute of Research in Silver Spring, Maryland. Advanced testing will be conducted at military medical research laboratories located in Peru, Kenya, Egypt, Indonesia, and Thailand.

The Hunt for the Next Best Mosquito Repellent

It is impossible to calculate how much illness, death, and misery has been prevented during the last 50 years by simple application of a bit of N, N diethyl-*m*-toluamide to exposed skin. Better known as DEET, it is the active ingredient in all the world's most effective and widely used mosquito repellents. Developed as a repellent for the military by ARS scientists in the mid-1950s, DEET is now used by an estimated 200 million people each year. Still, it has its drawbacks: Not all insect vectors are equally repelled; it can dissolve some plastics; and formulations for prolonging its activity on skin can be messy to apply.

Working with military counterparts, entomologist Jerome A. Klun and his colleagues at CAIBL have isolated and tested a possible replacement for DEET. Called "SS220," it's a stereoisomer from a mixture first synthesized by ARS scientists in 1978. ARS was issued a patent for SS220 in 2003. It is currently undergoing toxicology tests required for registration with the Environmental Protection Agency. Recent field tests show that 20 percent SS220 is as effective as 33 percent DEET in protecting troops against the major species of disease-carrying mosquitoes—and it does not dissolve plastics.

"This new repellent chemistry affords flexibility and choice for protection against a variety of disease vectors," says Klun. "The next challenge will be to find a long-lasting, odorless formulation for it that will encourage soldiers to use it routinely."

At CMAVE, chemist Ulrich Bernier and his colleagues have begun several other projects under the DOD initiative, including developing new formulations and looking at old formulations to be used as insect repellent compounds on skin. About 600 synthetic compounds related to piperdines, a repellent found in trace amounts in black pepper, were developed by Gainesville and Beltsville researchers in the mid 1970s and will now be researched further.

WRAIR (D203-1)

David A. Carlson, a CMAVE chemist, says, "We'll work with the University of Florida to re-examine the most promising compounds by carrying out structure-activity relationship studies using the old data and then testing candidates on cloth patches or in our olfactometer, one of only a few in the world. It's a specially designed piece of equipment that we use in the lab to test the reaction of mosquitoes and flies to a particular repellent. Possibly we can develop new candidates as we learn what works best."

Fabrics and Other Barriers Shield Troops From Insects

Millions of people—especially children—living in Asia, Africa, and Latin America are protected every night from bites of malaria mosquitoes by sleeping under bed nets that have been dipped in a special insecticide. This simple but

U.S. Army preventive medicine personnel treat uniforms with permethrin to ward off mosquitoes, sand flies, and other small insect pests.

effective method had its origin in the swamps of Florida, where in the 1960s Carl Schreck and fellow ARS scientists tested the concept of treating cloth to be used by soldiers. In a series of influential reports beginning in 1967, Schreck and his colleagues showed how treated clothing repelled mosquitoes, leading directly to current use of treated battle dress for soldiers and the nets for children.

But over the last 30 years, there have been changes that compromise the efficacy of treated cloth. The military uses some synthetic materials for tents and clothing because they're more durable, lighter, and more comfortable than cotton. But they're harder to treat by dipping or spraying. And mosquitoes are becoming resistant to pyrethroids, a family of low-toxicity compounds, originally purified from chrysanthemum flowers, which have both repellent and insecticidal actions.

At Kerrville, Texas, entomologists Mat Pound and Kim Lohmeyer of the Knipling-Bushland U.S. Livestock Insects Research Laboratory are investigating ways to reformulate the current pyrethroid treatment used by the military to maintain its activity beyond the current 10 to 15 washings. At CMAVE, Bernier and an industrial partner are studying how to infuse fabric with nonpyrethroid chemicals.

Prevention Is Only as Good as Its Application

In the early 1940s, two ARS engineers in Florida had a brainstorm. They needed to find an efficient way to propel a fine mist of insecticide for use by troops. A few years before, the DuPont Company had discovered a new, nontoxic refrigerant called "Freon," which had properties under pressure that now caught their attention. In 1941, L.D. Goodhue and W.N. Sullivan patented, on behalf of the Secretary of Agriculture, the prototype of the first aerosol can, christened the "bug bomb" by grateful soldiers.

There remains much need for innovative methods to deliver insecticides in just the right quantities to just the right places; the best control agent is useless if it can't be applied. In Kerrville, Texas, agricultural engineer Allen Miller is working with Pound and Lohmeyer to develop delivery systems that provide sustained release of repellents. They are studying polymers and mechanical dispensers that would permeate the closed environment of a tent or vehicle, preventing mosquitoes or sand flies from entering. A polymer, such as those used in air fresheners, would dispense the insecticide over a period of 2 to 3 months, while the mechanical dispenser would activate at a particular time overnight. At Gainesville, a collaboration has begun with Navy engineers to improve the efficiency of ultra-low-volume misting, another ARS invention for use by aircraft, including possibly unmanned drones, in combat zones.

Kenneth Linthicum, director of CMAVE, worked in Asia and Africa on mosquito-borne viruses like dengue and Rift Valley fever and in the United States on West Nile virus. He knows the importance of being prepared.

"The tools ARS develops for the military will be immediately accessible to civilians," Linthicum says. "The rapid spread of West Nile virus demonstrates the nature of the threat. In the war against infectious diseases, the weapons used by soldiers and civilians to defend themselves will be the same."—By **Jim Core, Rosalie Bliss,** and **Alfredo Flores,** ARS.

This research is part of Veterinary, Medical, and Urban Entomology, an ARS National Program (#104) described on the World Wide Web at www.nps.ars.usda.gov.

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